CHANGES IN NERVE CELLS AS A RESULT OF THE ACTION OF IONIZING RADIATION

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CHANGES IN NERVE CELLS AS A RESULT OF THE ACTION OF IONIZING RADIATION[1]

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The author conducted a histomorphological analysis of various central nervous system structures from roentgen-irradiated (500r) dogs. Three figures show histological changes in various neural tissues caused by irradiation. The mechanisms of these changes are discussed. The conclusion drawn from this study was that histomorphological changes in the nervous system reflect its sensitivity to ionizing radiation. Injury to neurons of the vas__omotor reflex arc should be considered relative to the general pathogenesis of radiation sickness and the hemorrhagic syndrome as reflecting disruption of vascular wall trophics.

The question of whether nervous system elements are particularly sensitive /1171* to the effects of ionizing radiation is still being discussed in the radiobiological literature. Investigations conducted during the 1920's and 1930's (refs. 1-5) led to the opinion that neural tissue in young animals is radiosensitive to penetrating radiation based on observable morphological changes. However, it developed that brain tissue in adult animals is also damaged. Contrary to this opinion, a number of investigators (refs. 6-8) hold that neural tissue is radioresistant despite consistently observable functional shifts in the nervous systems of irradiated organisms. Presently, a considerable number of morphological studies by foreign (refs. 9-16) as well as native investigators (refs. 17-28) allude to injury to nervous system structures as a result of ionizing radiations. In this respect, the study conducted by A. L. Shabadash (ref. 28) and his report to the Conference Dedicated to the Memory of A. A. Zavarzin (1959) deserves special attention.

It should be mentioned that the data of a number of investigations cannot always be subjected to comparison inasmuch as the periods of observations, species of animals used (the majority of investigations have been conducted on rodents), and conditions of irradiation have sharply differed; the need for further investigations in this area of radiobiology is therefore obvious.

The present investigation concerns a study of the dynamics of changes in neurons in some parts of the central nervous system of animals during various stages of experimentally induced radiation sickness.

Experiments were conducted on 15 male dogs exposed simultaneously from two sides to whole body roentgen radiation under the following conditions: 180 kV, 15 min, 6.3 r/min dose rate, 0.5 mm Cu + 1 mm Al filter, 120 cm skin-focal distance. The layer for 50 percent attenuation was 1 mm Cu. The radiation dose, measured in the air, was 500 r which corresponds to LD 50/30. Animals were killed at intervals ranging from 2 to 28 days after irradiation. Mortalities were not included. Three non-irradiated dogs served as biological controls. Ganglia of the peripheral sympathetic system (truncus sympatheticus) segments of the thoracic spinal cord with their corresponding spinal ganglia were

* Numbers in the margin indicate pagination in the original foreign text.
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histologically examined. Specimens were fixed in 96° alcohol and 10 percent neutral formalin. Celloidin sections stained with thionine (Nissl) and hematoxylin-eosin (van Hyson) were prepared. As a result of irradiation, the animals developed II and III degree acute radiation sickness with the characteristic clinical and anatomical symptoms. The crisis period of radiation sickness lasted for 10-21 days.

Tigroid material in the form of small bodies diffused throughout the entire structure of the majority of cells observed was uniformally distributed in the sensory nerve cells of the thoracic spinal ganglia. In the cytoplasm of individual neurons, there were small areas lacking this chromophilic substance, their contours resembled vacuoles; not infrequently there were very distended and perineuronal capsules around these neurons (fig. 1a). Vacuoles, some small and others large, were encountered in the body of the neurons. They were also encountered in elements of the surrounding glia. Pycnomorphous nerve cells were rarely noted. During the beginning of the radiation sickness crisis and throughout its entire course, portions of cytoplasm lacking Nissl material are discovered with considerably higher frequency than in the precrisis period. It is possible to observe moderate vacuolization of neurons, substantial chromatolysis, and at the end of the crisis period, neuron cytolysis as well. Occasionally, tigroid material appears to be concentrated in heavy bodies and situated either around the nucleus or around the periphery of the neuron. Separate or groups of heavily stained neurons are observed (fig. 1b) due to pycnotic changes. The nucleus in individual neurons is enlarged, weakly stained, and like a transparent bubble containing a large, heavily stained nucleus (fig. 1c).

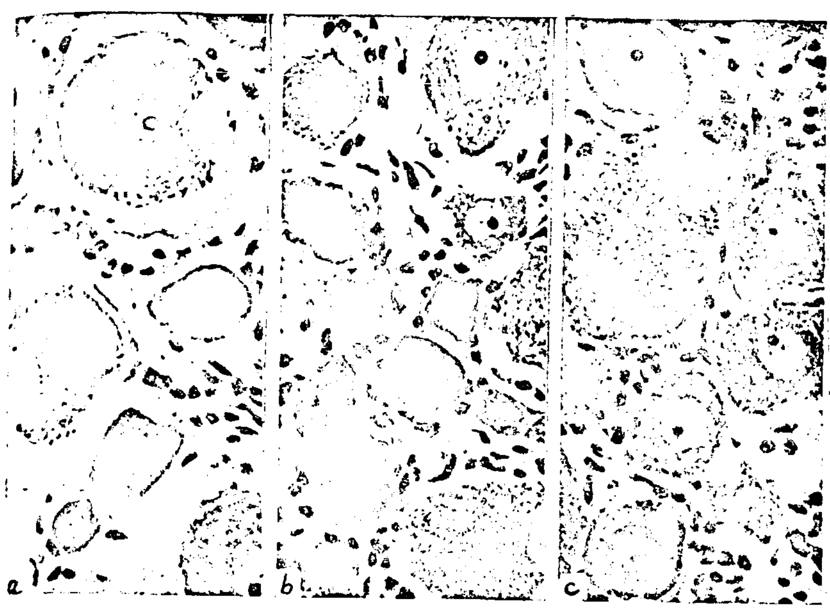

Figure 1. Neurons of the spinal ganglia of irradiated dogs. a. thionine stain- 4 days; a portion of neurons lacking Nissl material; distention of perineuronal capsules; b. 21 days; a focus of pycnotically convoluted cells; c. 27 days; nonuniform staining of neurons, nucleus swelling. ob. 40, ~10 x.

In small and medium sized neurons, isolated cases of hyperchromatosis and nuclear swelling (fig. 1c) is observed. A similar type of shift is frequently observed at the end of the crisis period of radiation sickness.

In cells of lateral horns of thoracic segments of the spinal cord ("sympathetic nuclei"), change in tigroid material is not observed in the majority of neurons. It is uniformly distributed in the cytoplasm of nerve cells in the form of small bodies. Only individual neurons lacking Nissl material and a few dead cells are encountered. During the crisis period of radiation sickness, and especially during its termination, Nissl material appears in the form of isolated, very heavy bodies, occasionally very uniformly distributed throughout the body of the neuron; in other neurons, the amount of chromophilic matter decreases (fig. 2), and finally, neurons absolutely lacking Nissl material are observed which remind one of "shadow cells". At the end of the crisis period and during the recovery of the animal from this period, the number of dead neurons becomes relatively large.

In motor neurons of anterior horns of spinal thoracic segments, a disruption in the distribution of tigroid material could not be observed at any time nor during any stage of radiation sickness studied. Evidently, these neurons are more resistant to the effect of ionizing radiation.

In nerve cells of the truncus sympatheticus, tigroid material was, as a rule, uniformly dispersed in minute, granulated form throughout the entire cytoplasm. The peripheral rim of the cytoplasm contained somewhat more tigroid material than the entire remainder of the cells. As the period after irradiation increased, the amount of tigroid material in the perinuclear zone decreased progressively while increasing along the cell periphery (fig. 3a). It creates a picture of central chromatolysis with peripheral hyperchromatosis. The nucleus in such cells is often displaced towards the periphery, enlarged, and very weakly stained. During the latent period of radiation sickness, only initial manifestations of Nissl coagulation is observed along the periphery with normal distribution occurring in the central portion of the cells.

Already at the beginning of the crisis period many neurons appear to be de- /1172
formed and their outlines become irregular, sometimes almost angular. Isolated neurons appear to be wrinkled. During this period, distinct manifestations of peripheral hyperchromatosis with central chromatolysis are observed. Among neurons which have undergone similar changes and nearly lack chromophilic material, only isolated hyperchromic nerve cells or groups of them are encountered
(fig. 3b); the cytoplasm of these cells is intensely stained by thionine. Ap- /1173
parently such neurons eventually undergo necrobiotic changes and die; remains of the disintegrated nerve cells are found among them. At the end of the crisis period of radiation sickness and during recovery, the mortality of nerve cells is also observed, occasionally accompanied by a proliferative reaction of the glia.

Experimental data indicate that in neurons of the autonomic vasomotor reflex arc: sensory spinal ganglia, lateral horns of thoracic segments of the spinal cord and of the truncus sympatheticus, all intimately involved with the regulation of vascular tonus and trophics, undergo significant shifts relative to the disposition and quantity of Nissl tigroid material which reflects the functional condition of the neuron.

Figure 2. Neurons of the lateral horns of a pectoral segment of the spine of an irradiated dog stained with thionine. 12 days. The amount of tigroid material is sharply decreased in one of the neurons (chromatolysis). ob. 60, ~10 x.

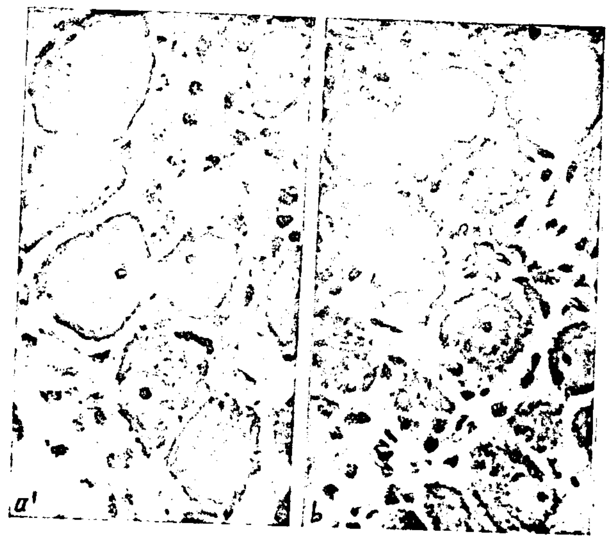

Figure 3. Neurons of ganglia of the truncus sympatheticus of irradiated dogs. a. 27 days; the disappearance of tigroid material from the center and its concentration along the periphery; nuclear displacement and enlargement; b. 17 days; a hyperchromic neuron among cells in a state of chromatolysis. ob. 40, ~40 x.

During the crisis period of radiation sickness, morphological changes in vascular walls and changes in the tigroid material of neurons become more distinct.

One factor which deserves particular attention should be stressed. Dead neurons are encountered in two different periods of radiation sickness: the first day after irradiation and at the end of the crisis period (or at the very beginning of recovery). Evidently, mortality in the first case is due to the direct effect of radiation. Mortality in the second case is due to sharp changes in metabolic processes during later periods of radiation sickness both as a result of the continuing direct effect of ionizing radiation and the possible after-effect of vascular disorders.

The observed morphological changes in the nervous system reflect the sensitivity of neurons to the effects of ionizing radiation; they agree with data described in the literature and supplement them.

Injury to neurons of the vasomotor reflex arc during exposure to penetrating radiation should be considered both in the light of the pathogenesis of radiation sickness as a whole and relative to the characteristic hemorrhagic syndrome caused by a disruption in vascular wall trophics.

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